REMARKS

Applicant thanks Examiner Woodward for the courtesy of conducting the telephonic interview with the undersigned attorney on December 4, 2007.

I. The Invention

The present invention describes a recombinant vector useful for inducing a tumor-specific immune response against B-cell lymphoma, by way of a fusion protein of a cytokine and a tumor-specific idiotype. Rather than directly encoding the fusion protein, which would require individual cloning of the idiotype of every patient's lymphoma cells, the expression vector of this invention includes a sequence of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron, such that, following transfection of a B lymphoma cell and subsequent homologous recombination, the DNA sequences coding a cytokine and a immunoglobulin constant region (or a part thereof) also present in the vector are incorporated into the malignant B cell's genomic sequence. A cytokine fusion protein is then produced by the B cell to include the specific idiotype encoded by the endogenous sequence of the malignant B cell. After rendered incapable of proliferation, such a malignant B cell expressing a tumor immunoglobulin-cytokine fusion protein can be reintroduced into a patient to elicit a specific anti-B cell lymphoma immunity due to enhanced recruitment of antigen-presenting cells by the cytokine and more effective presentation of the tumor-specific immunoglobulin idiotype. This invention eliminates the need to clone each patient's idiotypic domain and is thus quick, convenient, and less expensive.

II. Status of the Claims

Claims 1-5, 7-9, 11-17, and 29 are pending. Upon entry of the present amendment, claim 1 is amended to explicitly provide the minimal length of a segment of the μ intron or the *k* intron. Support for this amendment can be found, *e.g.*, on page 10, lines 8-9. No new matter is introduced.

III. Restriction Requirement

The Restriction Requirement mailed October 10, 2006, divided claims 1-17 and 25-30 into two Groups: Group I, claims 1-17, drawn to a vector; and Group II, claims 25-30, drawn to use of the vector. Applicant has elected the claims of Group I for prosecution. A closer review of the claims reveals, however, that claim 29, drawn to a malignant B cell comprising the vector of claim 1, has been erroneously included in Group II while it clearly belongs to Group I. As such, Applicant requested in the response of August 6, 2007, that the Examiner consider rejoining claim 29 with the elected claims for examination. Since the Office Action of October 18, 2007, does not contain a response to this request, Applicant hereby renews this request.

III. Claim Rejections

A. 35 U.S.C. §112, First Paragraph: Written Description

Claims 1-5, 7-9, and 11-17 remain rejected under 35 U.S.C. §112, first paragraph, for alleged inadequate written description. Applicant respectfully traverses the rejection.

According to the MPEP, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention at the time of filing. The pending claims are drawn to a vector for expressing immunoglobulin-cytokine fusion proteins in malignant B cells. The vector comprises the following components operably linked to each other: (a) a region of at least 1.5 kb that is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron; (b) at least one DNA sequence encoding a constant region of an immunoglobulin or a part of the constant region; (c) a DNA sequence encoding a cytokine; and (d) a marker gene that is selectable in eukaryotic B cells and contains a functional enhancer region. Applicant submits that, at the effective filing date of this application, all of these common components of the claimed vector were known and available to a person of ordinary skill in the art. An artisan upon reading the present disclosure would then reasonably conclude that the present inventor had in his possession these components and therefore the claimed vector.

On page 3 of the Office Action mailed October 18, 2007, the Examiner cites *University of Rochester v. G.D. Searles & Co.*, 69 USPQ2d 1886 (Fed. Cir. 2004) and *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. App. & Int. 2007), and argues that the written description requirement is not met merely by enabling one to practice the claimed invention. In other words, the Examiner argues that the written description requirement must be met by describing what the claimed invention is, not what the invention does. Applicant takes no issue with this position. It must be pointed out, however, that the fact pattern in this application is very different from that of *Rochester* or *Kubin*. In *Rochester*, the claims in question were directed to the use of a COX-2 inhibitor. Although the patent applicant provided a detailed, enabling description for a skilled artisan to identify such COX-2 inhibitors, they were neither known in the art nor named in the application. The court held that the written description requirement was not met. In *Kubin*, the application claimed a genus of nucleotide sequences encoding natural killer cell activation inducing ligand ("NAIL") polypeptides, which were purportedly new and were defined as having at least 80% identity to a reference amino acid sequence and binding to CD48. The specification provided two species of nucleic acids and three species of fusion polypeptides within the claim scope, but none of the exemplary NAIL sequences included any variation within the reference amino acid sequence. While acknowledging the teaching in the specification on how to make and test additional NAIL sequences within the claim scope, the Board ruled that the exemplary species did not sufficiently represent the claimed genus and that the application fails to provide adequate written description to show applicant had possession of the full scope of the claimed invention at the time of filing.

In clear contrast to *Rochester* and *Kubin*, this application claims a recombination vector, the components of which (a μ or k intron segment and its homologous sequence; a DNA sequence encoding a whole or partial antibody constant region; a DNA sequence encoding a cytokine; a B cell selectable marker gene and an enhancer) are all known in the art and also described in the specification. An artisan would have no doubt about the inventor's possession of the common components of the claimed vector and would therefore have no doubt about the

inventors' possession of the vector itself. Because of these important factual distinctions, it is inappropriate to apply the *Rochester* decision or *Kubin* decision in the present application.

The Examiner has also expressed concerns over the single species described in the specification as a representative for the claimed genus of vectors (see the paragraph bridging pages 3 and 4 of the Office Action). Applicant refers to MPEP §2163 II.A.3 (a) ii), where it is stated that "[w]hat constitutes a 'representative number' [for a claimed genus] is an inverse function of the skill and knowledge in the art" and that there are situations "where one species adequately supports a genus." In view of the advanced state of the art of molecular biology, particularly the abundance of knowledge and high level of technical skills in immunology, Applicant believes that the instant case is indeed a situation where a single species sufficiently supports a genus.

In short, Applicant believes that the instant application fully meets the written description requirement under 35 U.S.C. §112, first paragraph. It is therefore respectfully requested that the Examiner withdraw the written description rejection.

B. 35 U.S.C. §102

Claims 1-5, 7-9, 11, and 13-17 are rejected for alleged anticipation under 35 U.S.C. §102(e) by Polack *et al.* (U.S. Patent No. 6,521,449) and under 35 U.S.C. §102(b) by Mucke *et al.* (*Gene Therapy* **4**:82-92, Feb. 1997). Applicant respectfully traverses the rejections.

As an initial matter, the present application claims priority to German patent application No. 195 41 450, filed April 22, 1997, whereas the Mucke reference was published in February 1997. Thus, the Mucke reference is not citable under 35 U.S.C. §102(b).

Secondly, Applicant contends that not neither Polack nor Mucke provides all limitations of the pending claims. For instance, Applicant does not believe that the limitation of "a region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron" can be found in either of the two references. The Mucke reference also fails to provide the limitation of a DNA sequence encoding an antibody constant region or a part thereof.

As such, the references by Polack or Mucke cannot anticipate the pending claims. Withdrawal of the rejections under 35 U.S.C. §102 is therefore respectfully requested.

C. 35 U.S.C. §103

Claims 1-5, 7-9, 11-13, and 15-17 are rejected under 35 U.S.C. §103 for alleged obviousness over Polack in view of Levy and Gillies. Claims 1-5, 7-9, and 11-17 are further rejected under 35 U.S.C. §103 for alleged obviousness over Polack or Mucke in view of Mocikat (*Immunology* **84**:159-163, 1995). Applicant respectfully traverses the rejections.

In order to establish a *prima facie* showing of obviousness, three requirements must be satisfied: all limitations of a pending claim must be expressly or impliedly disclosed by prior art references; there must be a suggestion or motivation in the art for one skilled artisan to combine the limitations; and there must be a reasonable expectation of success in making such a combination. MPEP §2143. As discussed above, neither of the primary references by Polack *et al.* and Mucke *et al.* provide all limitations of the pending claims. On the other hand, the secondary references, Levy, Gillies, and Mocikat, are cited to provide teaching of a vector encoding an idiotype/GM-CSF fusion protein, a vector encoding a recombinant antibody-cytokine fusion protein, and a vector for homologous recombination at the Ig locus, respectively (see page 16 of the Office Action mailed March 5, 2007, and pages 9-10 of the Office Action mailed October 18, 2007). None of these three secondary references provide at least one missing element, namely the region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron as recited in (a) of claim 1. Without providing all claim limitations, the cited references cannot support a *prima facie* case of obviousness.

The Examiner points out that Mocikat *et al.* included of a 2.3 kb fragment of the mouse μ intron sequence in their recombination vector (the paragraph bridging pages 159 and 160 of the Mocikat reference), but has identified nothing, either in the cited references or in the general knowledge an artisan would possess, that would motivate the artisan to modify (and particularly to shorten) the 2.3 kb intron sequence. Furthermore, even if such motivation could be found, there still would be no reasonable expectation, prior to the completion of actual

experiments, that the homologous sequence of a shortened length (by more than 1/3) would be sufficient for a successful homologous recombination event. Without the requisite motivation or reasonable expectation of success, no *prima facie* obviousness is established.

Accordingly, the rejections under 35 U.S.C. §103(a) cannot be sustained.

CONCLUSION

In view of the foregoing, Applicant believes that all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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